REMARKS

This document is filed in reply to the Office Action dated May 12, 2005 ("Office Action").

Applicants have amended claims 1, 10, and 18 to more clearly set forth the claimed invention. Support for the amendment to claim 1 can be found, e.g., in original claim 10 and at page 15, lines 5-7, of the specification. Support for the amendment to claims 10 and 18 appears, e.g., at page 19, lines 19-27, of the specification. Applicants have also incorporated into claim 11 the language of claims 1 and 17, and have cancelled claims 16 and 17. No new matter has been introduced by these amendments.

Claims 1-15 and 18-46 are pending. Among them, claims 21-45 have been withdrawn from consideration for covering a non-elected invention. Claims 1-15, 18-20, and 46 are under examination. Reconsideration of this application is requested in view of the following remarks.

Information Disclosure Statement

The Examiner stated that the Information Disclosure Statement mailed on November 26, 2003 did not enclose a copy of one reference listed therein, i.e., Muramatsu *et al.* (Reference AL). See the Office Action, page 2, lines 9-14.

Applicants would like to point out that a copy of Muramatsu *et al.*, as well as copies of seven other references, were submitted with the Information Disclosure Statement and received by the U. S. Patent and Trademark Office. This is evidenced by a return receipt postcard from the Office of Initial Patent Examination (copy enclosed), acknowledging receipt of copies of all eight references. In any event, applicants submit herewith another copy of Muramatsu *et al.*, and request that the Examiner review this reference and provide an executed Form PTO-1449.

35 U.S.C. § 102

The Examiner rejected claims 1-20 and 46 for an alleged lack of novelty on various grounds. Applicants will address each ground below.

I

Claims 1-6, 8, 9, 11-14, 16, 19, 20, and 46 were rejected as being allegedly anticipated by U.S. Patent Application 20020031827 by Kanno *et al.* ("Kanno"), U.S. Patent No. 6,495,513 to Rueger *et al.* ("Rueger"), or U.S. Patent No. 5,843,741 to Wong *et al.* ("Wong"). See the Office Action, page 3, lines 4-5, page 6, lines 3-4, and page 7, lines 17-18. Applicants have (i) incorporated into independent claims 1 and 11 the language of claims 10 and 17, respectively, which were not rejected in view of the three references, and (ii) cancelled claims 16 and 17. Independent claims 1 and 11 will be discussed first.

Claim 1, as amended, covers a method of generating a morphogen composition from an extracellular matrix (ECM). The method includes (i) growing cells on a surface in a fluid under conditions and for a time sufficient to enable the cells to form an ECM; (ii) removing living cells from the surface and leaving the ECM on the surface; (iii) stimulating the ECM to release morphogens into the fluid; and (iv) collecting the fluid to form a morphogen composition. Claim 11, as amended, covers a morphogen composition comprising a plurality of morphogens including at least a fibroblast growth factor, or a transforming growth factor beta, or both. The composition is produced by a specific method.

Kanno describes electrically stimulating cells in a medium and collecting the medium for testing a growth factor (VEGF). Rueger describes a composition containing a morphogen. Wong describes a method for altering the proliferation, differentiation, or function of anchorage dependent cells on a surface of an electrically conducting polymer. The method includes applying a voltage. See the abstracts, respectively.

Applicants submit that none of these three references describes a method that includes removing living cells from a surface and leaving an ECM on the surface and stimulating the ECM, and not the cells, to generate the morphogen composition, as required in amended claim 1. To the contrary, all three references describe stimulating the cells not the ECM. In addition, the cited references fail to describe a composition that includes at least a fibroblast growth factor, or a transforming growth factor beta, or both, produced by the recited method as required in amended in claim 11. This is evidenced by the fact that the Examiner, in view of the three

references, did not reject original claims 10 and 17, which recite "removing cells from the extracellular matrix" (which is on a surface) and "fibroblast growth factor, transforming growth factor beta, or both," respectively.

In view of the amendments and remarks above, applicants submit that claims 1 and 11 are patentable over Kanno, Rueger, and Wong. Claims 2-6, 8, 9, 12-14, 19, and 20 depend from claim 1 or 11. Claim 46 covers a pharmaceutical composition comprising a morphogen composition of claim 11. At least for the same reasons set forth above, these dependent claims are also patentable over the three cited references.

II

The Office Action rejected claims 1-7, 11, 12, 16, and 17 as being allegedly anticipated by U.S. Patent No. 6,485,963 to Wolf *et al.* ("Wolf"). See the Office Action, page 5, lines 4-5.

Applicants have cancelled claims 16 and 17 and will discuss amended independent claims 1 and 11 first.

As mentioned above, amended claim 1 is drawn to a method that includes (a) removing living cells from a surface and leaving an ECM on the surface and (b) stimulating the ECM to release morphogens. According to the Action, Wolf describes a method of stimulating cells with an electrical current. In the stimulated cells, a number of genes are suppressed or enhanced. Applicants note that Wolf does not mention ECM, let alone removing living cells from a surface and leaving an ECM on the surface, as required in claim 1. Again, this is evidenced by the fact that the Examiner, citing Wolf, did not reject original claim 10, which recites "removing cells from the extracellular matrix." Thus, it is respectfully submitted that Wolf does not anticipate amended claim 1 or claims 2-7, which depend from claim 1.

Claim 11, as amended, covers a morphogen composition comprising a plurality of morphogens including at least a fibroblast growth factor, or a transforming growth factor beta, or both. The Examiner asserted that "Wolf teaches a method for stimulating cells with an electrical current ... The resulting morphogen composition is ... shown to contain a plurality of growth factors including fibroblast growth factor (column 18, line 24)" (See the Office Action, page 5, lines 13-17). Applicants note that, contrary to the Examiner's assertion, Wolf does not disclose

any fibroblast growth factor-containing composition. Instead, Wolf, at column 18, line 24, recites "fibroblast growth factor receptor," which differs from "fibroblast growth factor" recited in amended claim 11. In fact, Wolf does not mention either a fibroblast growth factor or a transforming growth factor beta, as recited in amended claim 11. Thus, claim 11 is not anticipated by Wolf. Neither is claim 12, which depends from claim 11.

Further, applicants have amended claim 11 to specify that morphogens in the claimed composition are released from a stimulated ECM. Wolf does not describe making any ECM much less stimulating the ECM and obtaining morphogens from the stimulated ECM. Thus, claims 11 and 12 are patentable over Wolf on this independent ground.

III

Claims 1-5, 10-12, 15-18, and 46 were rejected as being allegedly anticipated by U.S. Patent Application by Stringer *et al.* ("Stringer"). See the Office Action, page 7, lines 1-2. Claims 16 and 17 have been cancelled and independent claims 1 and 11 will be discussed first.

According to the Examiner, Stringer describes every step of the method of claim 1. More specifically, the Office Action states that "Stringer teaches a morphogen composition and a method of forming it wherein the steps include culturing cells, harvesting the extracellular material produced by the cells (which removes the cells), isolating and purifying the material, and lyophilizing the material." See the Office Action, page 7, lines 10-13.

Applicants note that claim 1 requires a step of stimulating an ECM to release morphogens into a fluid. Stringer fails to describe any stimulation step. In addition, the claimed method requires a step of removing living cells from a surface and leaving the ECM on the surface. Stringer does not teach this step either. Instead, Stringer describes growing cells in a medium in a culture dish and harvesting materials from the medium. During this process, the cells are maintained on, but not removed from, the surface of the dish. See page 9, paragraphs [0175]-[0180]. For these reasons, contrary to the Examiner's statement, Stringer does not describe every step of the method of claim 1, and therefore does not anticipate claim 1.

Claim 11, as amended, is drawn to a morphogen composition prepared by a method including (a) removing living cells from an surface and leaving the ECM on the surface and (b)

stimulating the ECM to release morphogens. As discussed above, Stringer fails to describe such a method. In addition, Stringer fails to recite a composition including at least an FGF or a TGFβ released from an ECM. Thus, for these reasons, claim 11 is not anticipated by Stringer.

Claims 2-5, 10, 12, 15, 18, and 20 depend from claims 1 or 11. Claim 46 covers a pharmaceutical composition comprising the morphogen composition of claim 11. At least for the same reasons above, these claims are also patentable over Stringer.

CONCLUSION

Applicants submit that grounds for the rejections asserted by the Examiner have been overcome, and that the pending claims define subject matter that is patentable. As a result, applicants submit that allowance of this application is proper, and request an early favorable action. Please apply any other charges to deposit account 06-1050, referencing Attorney Docket No. 08688-057001.

Respectfully submitted,

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Applicant Susan J. Braunhut et al.			
Enclosures ·Information Disclosure Statement (1 page) ·Form PTO-1449 (1 page) ·Documents listed on the Form PTO-1449 (8 documents)